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13. ABSTRACT (Maximum 200)  The present study examined the effects of a presurgical psychosocial intervention for breast cancer patients on immune function. Forty-nine patients were randomly assigned to either a control (standard care) or an intervention group (standard care plus psychosocial intervention). The two-session intervention included: 1) relaxation techniques; 2) problem-solving and crisis management; 3) psychosocial support; and 4) health education. Natural killer (NK) cell cytotoxicity and interferon-gamma (IFN- $\gamma$ ) production by peripheral blood mononuclear cells were examined at three time points. While NK cell cytotoxicity did not reliably vary as a function of time or treatment group, a significant interaction (Treatment X Time) was noted for IFN- $\gamma$ ( $F=5.81$ ; $p<.01$ ). Closer examination revealed that IFN- $\gamma$ levels declined significantly in controls over the course of the study, while intervention group IFN- $\gamma$ levels actually increased. Mirroring the IFN- $\gamma$ results, psychological assessment indicated that the intervention had a positive emotional impact on patients. Despite a number of methodological and interpretational difficulties, the present findings suggest that a brief, presurgical intervention may successfully enhance IFN- $\gamma$ (a critical cytokine for cell-mediated immune responses) production in breast cancer patients.					
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Jan Moynihan 2-11-99  
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## TABLE OF CONTENTS

	<u>page(s)</u>
Front Cover . . . . .	1
Standard Form 298 . . . . .	2
Foreword . . . . .	3
Introduction . . . . .	5-7
Body . . . . .	7-19
Summary and Conclusions . . . . .	19-20
References . . . . .	21-26
Figure 1 . . . . .	27
Figure 2 . . . . .	28
Final Report Bibliography, etc. . . . .	29

## INTRODUCTION

Impending surgical procedures often generate a great deal of psychological distress (1,2), a fact which is clearly exemplified by the intense distress frequently experienced by women who have been diagnosed with breast cancer (3,4). In addition to the obvious physical stress of surgery, breast cancer patients report experiencing a host of negative emotions, including anger, fear, and hopelessness. Recent psychoneuroimmunology research illustrates that across a variety of stressful situations, negative emotional responses are often paralleled by potentially deleterious alterations of the immune system (5-8). Such findings have led a number of researchers to the conclusion that reducing psychological distress may actually help to enhance both reactions to and recovery from surgery by upregulating immune function (1,9-13). However, little is known about the immunological consequences of such interventions with breast cancer patients. In addition, breast cancer interventions have traditionally been implemented post-surgically, after the acute crisis of the surgical procedure itself has passed. The present study therefore examines the usefulness, from an immunological perspective, of a focused, pre-surgical psychosocial intervention for breast cancer patients.

A good deal of evidence has been collected which links the experience of stress with depressed immune function, including reduced natural killer (NK) cell cytotoxicity (7, 14-16). NK cells are large, granular lymphocytes which kill pathogen-infected and tumor cells in a nonspecific fashion, and may play an important role in the early control of tumor development (17-20). NK cell activity is augmented by cytokines, such as interferon-gamma (IFN- $\gamma$ ), which is produced by T cells and NK cells themselves. Researchers studying breast cancer patients have most often found a significant suppression of NK cell function in such patients when compared to controls (21-24), and in at least one study a similar suppression of IFN- $\gamma$  was noted

(25). However, the role that stress may play in either the initiation or maintenance of this suppressed immune response in breast cancer patients remains largely unexplored. Data from Levy et al. (26, 27) support the idea that depressed NK cell activity in breast cancer patients may be related to psychological distress. In addition, Andersen and colleagues (28) recently examined 116 women who had previously undergone breast cancer surgery, concluding that higher levels of stress significantly predicted lower NK cell lysis and diminished NK cell response to recombinant IFN- $\gamma$  in vitro.

Breast cancer researchers who have attempted to link stress with immune function have customarily proceeded by assessing patients after surgery for breast cancer has already taken place, rather than during the period prior to surgery. However, Kiecolt-Glaser et al. (1) and others (29, 30) note that the amount and severity of psychological distress which is experienced prior to surgery may actually be most predictive of the postoperative recovery experience, and that this relationship seems to be mediated in part by suppression of the immune system. People who are highly anxious prior to surgery have poorer outcomes, including more intense postoperative pain, more frequent postoperative complications, and longer hospital stays, than those who are not as anxious. Interestingly, immune function in breast cancer patients during the presurgical period has been shown to be suppressed, including both NK cell activity (23, 24) and IFN- $\gamma$  production (25), although these studies have been somewhat inconsistent (31). These results suggest that the psychological distress which is experienced by breast cancer patients during the period between diagnosis and surgery (i.e., the presurgical period) may be directly related to a predictable suppression of immune function. Clearly, suppression of the immune system during the perioperative period, when the risk of infection is at its peak, is less than ideal. Moreover, this immune suppression may then also serve to negatively influence the process of recovery from surgery.

Because psychological distress and immune suppression are related, it stands to reason that interventions designed to help manage and reduce psychological distress might also result in the upregulation of immune function. A variety of structured psychosocial interventions have been used to treat cancer patients, and many of these interventions have empirically been shown to offer such patients a wide range of emotional and physical benefit. For example, psychosocial interventions have been shown to improve the psychological well-being of breast cancer patients (32-36), and even to increase the length of survival for both advanced metastatic breast cancer patients (34, 37) and stage I and II melanoma patients (11, 38). Interestingly, all such interventions have traditionally been implemented post-surgically. However, given the fact that the pre-surgical period is known to elicit a variety of stressful feelings, as well as the fact that such stress has been shown to decrease some aspects of immune function, it is likely that a focused, pre-surgical psychosocial intervention for breast cancer patients would enhance immune function.

In the present study, we examined the relationship between psychological distress and immune function in breast cancer patients using a two-session psychosocial intervention. In particular, we hypothesized that breast cancer patients who participated in the intervention would have improved immune function, as measured by an increase in both NK cell activity and IFN- $\gamma$  production, when compared to breast cancer patients who did not receive the same intervention.

## METHODS

### *Sample*

Participants were 49 women who ranged from 29 to 80 years of age (mean age = 56 years). All women had been diagnosed with breast cancer just prior to enrollment, and were awaiting either surgery, or surgery plus radiation or

chemotherapy. Because of enrollment concerns, no attempt was made to control for breast cancer stage. All participants were volunteers who were recruited from local surgical practices over a period of approximately 18 months. The vast majority of the women (98%) were Caucasian. Due to potential immunologic confounds, volunteers were excluded if they had given birth within the past three months; if they reported an infectious illness within the past two weeks; or if they were taking medications with obvious immunological consequences (e.g., steroids). Because of intervention scheduling constraints, volunteers were also excluded if their surgeries were scheduled to take place within one week of breast cancer diagnosis.

### *Design*

A pretest-posttest control group design was used (39). Volunteers were randomly assigned to either a control group (N=27) or an experimental group (N=22). The method of restricted randomization was used to help equalize the number of volunteers assigned to each of the two groups. Control group members received standard breast cancer care; experimental group members received standard care plus a two-session psychosocial intervention. Psychological assessments were administered, and blood samples were collected from these patients at three time points: within 72 hours of diagnosis, and prior to the intervention (Time 1); following the intervention, but immediately before surgery (Time 2); and one week following surgery (Time 3). The original sample included 51 women; two women (both controls) dropped out after the first time point, and these data were eliminated. Occasional data points at any given time were also incomplete or missing for reasons which included: patient error (e.g. questionnaires filled out incorrectly or incompletely); patient unwillingness to allow blood to be drawn; inability to obtain an adequate blood sample; and laboratory errors.

### *Intervention*

Each participant in the experimental group attended two, 90-minute treatment or "intervention" sessions. Due to the slow rate of referral and the brief window of opportunity between diagnosis and surgery, most interventions were conducted individually, though a few consisted of small groups (2-3 patients). Group size was determined by the rate of patient referrals in any given week. All interventions were led by one of two clinical psychologists, each of whom was trained to conduct the intervention in a standardized manner, using a written protocol and a variety of predetermined intervention techniques (described below). All interventions were held in designated group therapy rooms in the Department of Psychiatry at the University of Rochester Medical Center. The intervention design was consistent with findings and recommendations from previous treatment research with cancer patients (38, 40), indicating that newly diagnosed and early treatment stage patients are responsive to highly structured interventions. The objectives of the intervention were: 1) to offer psychosocial support through discussion with the leader (and, if applicable, with other group members) about specific problems and concerns commonly faced by breast cancer patients; 2) to improve problem-solving skills required for effective crisis management; 3) to teach and practice relaxation and stress management techniques; and 4) to increase education about improving and maintaining proper health habits.

The intervention began with an introduction which included an overview of the structure and purpose of the intervention, the specific agenda for that particular day, and assurances that patient confidentiality would be maintained. On the first intervention day, each patient initially discussed with the leader such topics as: 1) when she was first diagnosed with breast cancer; 2) when she would be having surgery (and what type); 3) the impact (emotional or otherwise) that the diagnosis may have had on significant others in her life; and 4) the specific impact that the

diagnosis and impending surgery may have had on the patient herself. The role of the leader during this discussion was to lend psychosocial support to the patient, while simultaneously asking questions which helped to identify patient problems or difficulties that might warrant further attention. Once the initial discussion concluded, the intervention leader presented patients with concrete information about stressful life events, including the universality of the experience of stress and the effects of stress on the body (physical, cognitive, emotional, and behavioral). This presentation then led into a discussion of problem-solving strategies, which were individually tailored to address the specific concerns raised by each patient. During the final thirty minutes of the intervention, patients were presented with an introduction to progressive muscle relaxation, and led through an exercise in the same. At the end of the first intervention session, each patient was given a cassette recording of this exercise, and was instructed to practice the exercise twice daily. The session concluded with patient debriefing and the completion of a feedback questionnaire.

The second intervention session followed the same general format as the first session. The initial discussion consisted of a follow-up to what had been discussed during the previous session, and patients were asked to identify any continuing emotional difficulties or obstacles they might be facing as surgery approached. During the second session, patients were also asked whether or not they had been consistently practicing the progressive muscle relaxation exercise, and were once again guided through the exercise at the end of the session. As with the first, the second session concluded with patient debriefing and the completion of a feedback questionnaire.

### *Psychological measures*

Measures of psychiatric distress included the Center for Epidemiological

Studies-Depression scale (CES-D), a 20-item measure of depression that places relatively little emphasis on physical symptoms (41); the Differential Emotions Scale-IV (DES-IV), a 36-item measure which is divided into 12 subscales, each thought to measure one aspect of an individual's emotional experience (42); and the Impact of Event Scale (IES), a 15-item measure of intrusive and avoidant thoughts and actions (43). High scores on the IES have been found to significantly predict lower NK cell lysis and diminished response of NK cells in vitro to recombinant IFN- $\gamma$  (28).

Other questionnaires included the Life Orientation Test, an 8-item measure of global optimism previously used in research with breast cancer patients (44); and the SF-36, a widely used health survey derived from the Medical Outcome Study (45) which was used to gather background medical data.

#### *Isolation of peripheral blood mononuclear cells (PBMC)*

Peripheral blood mononuclear cells (PBMC) were isolated from 30 ml of diluted, heparinized blood by centrifugation over Ficoll-Hypaque (Pharmacia, Piscataway, NJ). PBMC at the interface were washed twice, counted, and resuspended to  $5-10 \times 10^6$  cells/ml in fetal bovine serum (FBS). To assess immune function in PBMC from all three study time points simultaneously, cells were frozen at  $-80^\circ\text{C}$  according to the protocol of Vingerhoets et al. (46). At the time of assay, aliquots of cells were washed twice and resuspended to  $10^7$  cells/ml in RPMI-1640 medium containing 10% FBS, 2 mM L-glutamine, 50 mM 2-mercaptoethanol, 25 mM HEPES, 100 U/ml penicillin, and 100 mg/ml streptomycin sulfate (complete RPMI, all reagents from GIBCO, Grand Island, NY).

#### *NK cell activity.*

A standard  $^{51}\text{Cr}$  release assay using the K562 cell line (ATCC, Rockville, MD)

was used to measure NK cell activity (47). Effector cells were mixed in complete RPMI with  $^{51}\text{Cr}$ -labeled target cells at effector to target (E:T) cell ratios of 100:1, 50:1, 25:1, and 12.5:1. Supernatants were harvested following a 6-hour incubation in 5%  $\text{CO}_2$  at  $37^\circ\text{C}$  and counted in a gamma counter (WALLAC Oy, Finland). Statistical analyses were conducted to determine percent specific lysis for all four E:T ratios. Regression analysis confirmed that data from all four E:T ratios followed a linear progression at all three times points (all  $r$ 's  $\geq .993$ ). As a result, percent lysis values were standardized arbitrarily at the 50:1 dilution, so that individual values could be compared across Times 1-3 for all participants.

*Interferon-gamma (IFN- $\gamma$ ) production.*

IFN- $\gamma$  levels in culture supernatants were all assayed by enzyme-linked immunosorbent assay (ELISA). Briefly, 96-well plates were coated (50  $\mu\text{l}$ /well) with 2  $\mu\text{g}/\text{ml}$  purified anti-cytokine capture monoclonal antibody (mAb) (PharMingen, San Diego, CA) overnight at  $4^\circ\text{C}$ . Plates were decanted, blotted and blocked for two hours with 10% fetal bovine serum (FBS) in phosphate buffered saline (PBS) at room temperature. After decanting and blotting the plates, 50  $\mu\text{l}$  of sample in duplicate was added to the plate. Recombinant cytokine was used as the standard. After overnight incubation at  $4^\circ\text{C}$ , and after all subsequent steps, plates were washed three times with PBS containing Tween 20. The appropriate biotinylated anti-cytokine detecting mAb (1 $\mu\text{g}/\text{ml}$ , PharMingen, San Diego, CA) in 10% FBS, 0.05% Tween 20/PBS was added (50  $\mu\text{l}$ /well) and plates were incubated for one hour at room temperature. Avidin-peroxidase (Sigma Chemical Co., St. Louis, MO) at 2.5  $\mu\text{g}/\text{ml}$  in 10% FBS, 0.05% Tween 20/PBS was added (50 $\mu\text{l}$ /well) and incubated for 30 minutes at room temperature. Finally, 2,2'-Azino-bis(3-ethylbenzthiazoline-6-sulfonic) acid (ABTS; Sigma Chemical Co., St. Louis, MO) was added to the plates (100  $\mu\text{l}$ /well) and the absorbance of the color reaction measured at 405 nm.

### *Analytic Plan*

First, to assure that group randomization was achieved, preliminary analyses used unpaired t-tests and/or chi-squared procedures to look for group differences in age, marital status, number of children, level of education, employment status, and income. Next, to assess the effects of treatment on immunity, groups were contrasted using 2 (Group: treatment vs. control) X 3 (Time: Times 1-3) repeated measures analyses of variance (ANOVAs) separately for both NK cell activity and IFN- $\gamma$  level. When significant between-group differences were noted at baseline (i.e. Time 1) for either immune parameter, these values were then added into subsequent analyses as a covariate. Treatment effects on psychological variables were also assessed directly by examining changes in score over time. However, because we were specifically interested in assessing psychological changes due to the treatment, and we expected questionnaire responses at Time 3 to vary significantly from responses at Times 1 and 2 (due to the often overwhelming relief that patients feel once surgery is over), these assessments were conducted by simply examining changes in psychological response from Time 1 to Time 2 using paired t-tests for each group (treatment and control). Finally, supplemental analyses also utilized paired t-tests to examine changes in psychological variables following surgery (Time 1 vs. Time 3) for each group.

## RESULTS

### *Preliminary Analyses*

Preliminary analyses indicated that the treatment and control groups (N=49) did not significantly differ in terms of age, marital status, number of children, level of education, employment status, or total family income (all p's=NS). The "average" patient was approximately 56 years old (mean age= 55.9 years, SD= 13), married, had two children, had received at least some college education, was

employed full-time, and had a total family income which fell between \$50,000-\$75,000 per year.

### *Effects of Treatment on Immunity*

Group differences in NK cell activity were examined using a 2 (Group: treatment vs. control) X 3 (Time: Times 1-3) repeated measures analysis of variance (ANOVA). Due to missing values, only a subset (total N=22; controls=8, treatment=14) of the total sample was available for this analysis. No significant main effects for Time ( $df=2$ ;  $F=1.58$ ;  $p=NS$ ) or Group ( $df=1$ ;  $F=.02$ ;  $p=NS$ ) were noted, nor was the interaction term significant ( $df=2$ ;  $F=1.42$ ;  $p=NS$ ). Means and standard errors for this analysis are shown in Figure 1.

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Insert Figure 1 about here

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A similar repeated measures ANOVA conducted on IFN- $\gamma$  levels (total N=17; controls=6, treatment=11) revealed that the main effect for Time approached, but did not achieve, statistical significance ( $df=2$ ;  $F=2.65$ ;  $p=.09$ ). The main effect for Group also did not achieve significance ( $df=1$ ;  $F=.002$ ;  $p=NS$ ). However, a significant interaction between these two factors was noted ( $df=2$ ;  $F=5.81$ ;  $p<.01$ ). Closer examination of the means for each group (see Figure 2) indicated that IFN- $\gamma$  levels decreased steadily in the control group over time, while IFN- $\gamma$  levels in the treatment group appear to have actually increased slightly.

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Insert Figure 2 about here

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Examination of Figure 2 also reveals that baseline (Time 1) IFN- $\gamma$  levels significantly differed between the two groups ( $df=15$ ,  $t=2.309$ ,  $p<.04$ ). As a result, we conducted a second analysis on these data, this time using a repeated measures analysis of covariance (ANCOVA) so that these baseline IFN- $\gamma$  levels could be entered as a potential covariate. This analysis revealed that the Group X Time interaction was no longer significant ( $df=1$ ;  $F=0.8$ ;  $p=NS$ ).

### *Effects of Treatment on Questionnaire Data*

Comparing results from the CES-D, IES, DES-IV and LOT from Time 1 to Time 2 (before and after the intervention--both time points prior to surgery), we observed that subjects in the treatment group experienced significant increases in two subscales of the DES-IV, one measuring interest ( $df=14$ ,  $t=2.70$ ,  $p<.02$ ), and one measuring enjoyment ( $df=14$ ,  $t=2.43$ ,  $p<.03$ ). This was not true of the control group (both  $p$ 's= $NS$ ). In addition, subjects in the treatment group experienced a significant increase in a measure of optimism derived from the LOT ( $df=15$ ,  $t=2.16$ ,  $p<.05$ ), while controls did not ( $p=NS$ ). Finally, a DES-IV subscale measuring cancer-related disgust was found to significantly increase from Time 1 to Time 2 for controls ( $df=11$ ,  $t=3.53$ ,  $p<.005$ ), while the same was not true for those in the treatment group ( $p=NS$ ). No significant differences were found between Time 1 and Time 2 scores on the CES-D or the IES for either group.

### *Supplemental Analyses*

Examining changes in the questionnaire data from Time 1 to Time 3 (baseline to post-surgery), the sample as a whole (both groups) showed significant decreases in scores on the CES-D ( $df=33$ ,  $t=2.24$ ,  $p<.04$ ); DES-IV subscales measuring sadness ( $df=30$ ,  $t=3.86$ ,  $p<.001$ ) and fear ( $df=30$ ,  $t=3.75$ ,  $p<.001$ ); and overall scores for the IES ( $df=32$ ,  $t=3.93$ ,  $p<.0005$ ), as well as for the IES subscale measuring intrusion ( $df=33$ ,

$t=3.11$ ,  $p<.005$ ). In addition, all participants evidenced significant increases in DES-IV subscales measuring interest ( $df=29$ ,  $t=3.45$ ,  $p<.005$ ) and enjoyment ( $df=30$ ,  $t=3.61$ ,  $p<.005$ ). The overall decrease in CES-D scores from Time 1 to Time 3 appears to have been driven primarily by decreases in the control group ( $df=14$ ,  $t=2.50$ ,  $p<.03$ ), as Time 1 to Time 3 differences in the treatment group were not significant. No other between group differences were noted.

## DISCUSSION

The present study was designed to evaluate the potential immunologic benefit of a presurgical psychosocial intervention for breast cancer patients. To our knowledge, this is the first time that such an intervention has been attempted during the brief window of opportunity between breast cancer diagnosis and breast cancer surgery. As a result, the present findings are simultaneously both promising and somewhat limited. To be sure, implementation of this study was methodologically and logistically difficult. Consequently, our hope is that future research in this area may be guided not only by the content of our findings, but also by the process through which these results were obtained.

### *Immune and Psychological Findings*

Analysis of natural killer (NK) cell activity did not yield any significant differences between the control and the experimental groups. While overall NK cell activity levels during Time 1 and Time 2 (pre-surgery) appear to be somewhat lower than NK cell activity levels at Time 3 (see Figure 1), this difference did not achieve statistical significance. In general, this may be due to a limited sample size, as missing data made it necessary to limit our analysis to less than half of the patients in the original sample. The few studies which have demonstrated stress-related NK changes in breast cancer patients have typically been implemented

postsurgically and with larger samples (e.g., 28), making between-study comparisons difficult. In any case, in the present sample, no evidence of stress-induced suppression of NK cell activity was found, nor do the results support the idea that the presurgical psychosocial intervention in any way influenced the NK cell response.

More promising were the results obtained from PBMC stimulated with anti-CD3 to measure interferon-gamma (IFN- $\gamma$ ). IFN- $\gamma$  levels decreased substantially over time in the control group, consistent with the findings of Elsasser-Beile et al. (25) who demonstrated a suppression of IFN- $\gamma$  in breast cancer patients. However, this was not the case for the intervention group. Instead, IFN- $\gamma$  levels in the intervention group actually increased slightly over time. These data suggest that the intervention may have been successful in reducing the process of stress-related immunosuppression prior to surgery. These results are particularly interesting when one considers that the sample included in this analysis was again less than half the size of the original patient sample. Unfortunately, this finding is also clouded by the difference between IFN- $\gamma$  levels at baseline (Time 1), and the failure of this analysis to achieve statistical significance when these baseline differences were used as a covariate. Attempts to examine the data for significant differences between these two groups came up empty-handed. Thus, it remains unclear why control group levels were higher than intervention group levels at baseline. However, it should be noted that when one examines the shifts in data over time (see Figure 2), the pattern completely inverts, such that by Time 3, IFN- $\gamma$  levels are clearly lower in the control group than they are in the intervention group. Therefore, the present results cannot simply be due to the phenomenon of regression to the mean, and treatment effects cannot be entirely discounted.

Paralleling changes in IFN- $\gamma$  level, responses to psychological assessment indicate that the intervention had a positive emotional impact on breast cancer

patients. Specifically, when comparing scores before and after the intervention, patients in the intervention group became more interested and optimistic about their cancer, and generally expressed more enjoyment than they had previously, all of which were positive changes. Meanwhile, the only notable change in the control group was an increase in cancer-related disgust, which was clearly a negative emotional change. As expected, both groups experienced significant positive emotional shifts in score across a number of parameters following surgery (Time 1 compared to Time 3), which was simply interpreted as a testament to the intense relief felt by all concerned to have successfully completed the surgery itself.<sup>1</sup>

### *Methodological Limitations*

One major drawback of the present study is the potential for bias inherent in the patient recruitment process. For example, in order for a patient to be included, she first had to be referred to our experiment by a physician. None of the surgical practices from which patients were recruited referred 100% of patients awaiting breast cancer surgery. Therefore, it is clear that at some level, physician judgments were made regarding which patients were most "appropriate" for participation, thus leaving open the possibility that the present sample was biased and not representative of breast cancer patients in general. In addition, once patients were referred for the experiment, many still opted not to participate (roughly 50%), again leaving open the question of whether or not there were substantial differences between those who chose to participate and those who did not. Finally, the present sample was also limited by simple time factors. Specifically, those patients for whom surgery was scheduled less than a week after breast cancer diagnosis could not be included, because there was not adequate time to experimentally intervene.

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<sup>1</sup> The patients in the present study will also be assessed at six months post-surgery to see if these changes (as well as the changes in IFN- $\gamma$  level) will continue through the process of recovery.

This means that in some cases, those patients in most dire need of surgery (e.g. those with the biggest or most aggressive tumors) could not be included.

Another problem with the present study is the large amount of missing or incomplete data, which was due to both patient- and experimenter-related variables. Women undergoing breast cancer surgery indeed experience a good deal of emotional distress, and at times this distress had an impact on the data collection process. For example, patients filled out some questionnaires at home, which were then to be mailed back to the experimenters upon completion. In some instances, questionnaires which were intended to be filled out and returned prior to surgery were not actually filled out until after surgery. These data, obviously, could not be included in our analyses. Those patients whose questionnaires were tardy tended to cite emotional and time-related concerns as reasons for not completing the questionnaires. Patient distress also contributed to missing immune data. Specifically, some patients who initially agreed to participate in the study became less willing to consent to multiple blood draws as surgery neared.

### *Summary and Conclusions*

The present study represents an initial attempt to evaluate the potential immunologic benefit of a presurgical psychosocial intervention for breast cancer patients. Though the results must be interpreted with care due to a number of potential sample biases, as well as due to the small size of the present sample, the findings are nonetheless interesting. Examination of the immune data revealed evidence of stress-related suppression of IFN- $\gamma$  level in the control group. However, this immunosuppression did not occur in the patients who participated in the intervention, indicating that the intervention may have played a role in reducing both levels of stress and stress-induced immunosuppression of IFN- $\gamma$ . In contrast, the same pattern did not hold true for NK cell activity for either group.

Findings related to psychological assessment generally paralleled the IFN- $\gamma$  findings, as patients in the intervention group evidenced positive emotional shifts (i.e. became more optimistic and interested, and had higher levels of enjoyment) following the intervention, while control patients instead shifted a bit toward the negative (only exhibiting an increase in cancer-related disgust). It is hoped that these findings, as well as the difficult process by which they were obtained, will help first to highlight the need for psychosocial intervention prior to surgery, and also to guide researchers interested in implementing such interventions in the future.

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Figure 1

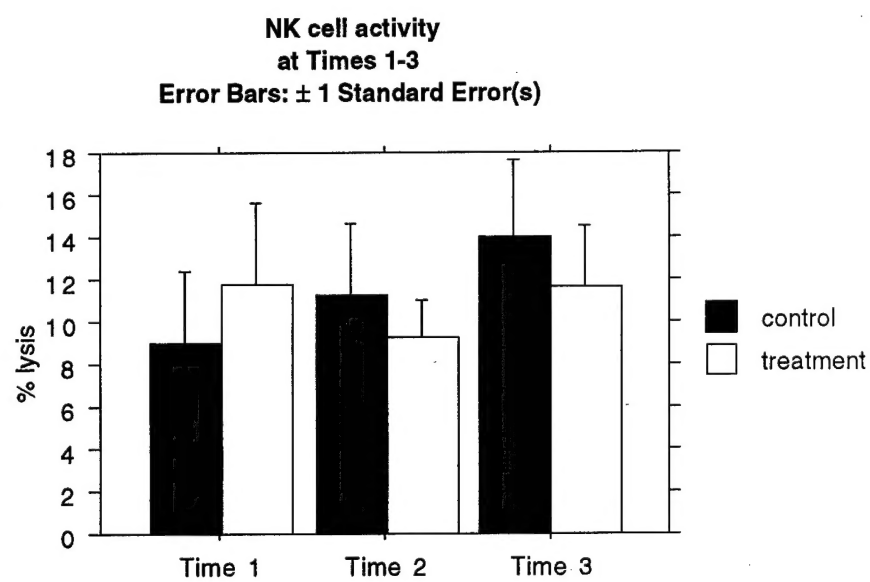
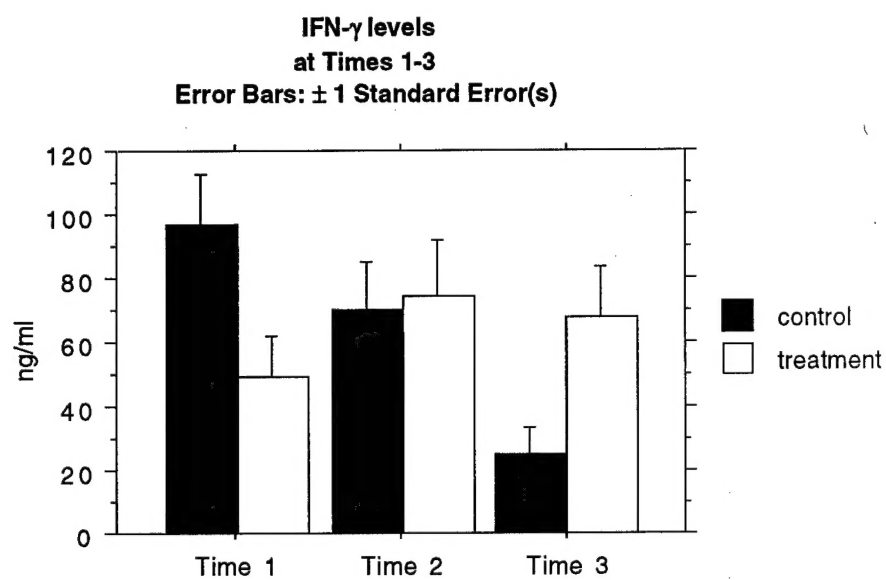


Figure 2



Final report bibliography and list of personnel receiving compensation from this effort:

*Abstracts*

- 1) Larson, M. R., Duberstein, P. R., Talbot, N., Caldwell, C., Frazer, H., & Moynihan, J. A. (1998). Effects of psychosocial intervention in women following breast cancer diagnosis. Poster presented at the nineteenth annual meeting of the Society of Behavioral Medicine, March 25-28, 1998, New Orleans, Louisiana. Poster also presented at the University of Rochester Cancer Center's 3rd Annual Scientific Symposium, Sept. 15, 1998, Rochester, New York.
- 2) Larson, M. R., Duberstein, P. R., Talbot, N., Caldwell, C., Frazer, H., & Moynihan, J. A. (1998). Psychosocial intervention following breast cancer diagnosis enhances interferon-gamma production. Poster accepted for presentation at the twentieth annual meeting of the Society of Behavioral Medicine, March 3-6, 1999, San Diego, California.

*Personnel receiving compensation from this project*

- 1) Jan Moynihan, Ph.D.--principal investigator
- 2) Heather Frazer--Health Project Coordinator

*Other*

Jan A. Moynihan, Ph.D. attended the Department of Defense's "Era of Hope" breast cancer meeting in Washington, D.C. in November of 1997.